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Applicants : William C. Olson, et al.

JUN 26 2000

Serial No. : 09/464,902

Art Unit: 1643 TECH CENTER 1600/2900

Filed : December 16, 1999

For : SYNERGISTIC INHIBITION OF HIV-1 FUSION AND
ATTACHMENT, COMPOSITIONS AND ANTIBODIES
THERETO1185 Avenue of the Americas
New York, New York 10036
June 19, 2000Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the PTO-1449 form attached hereto as Exhibit A. Copies of these references are attached hereto as Exhibits 1-31, respectively.

1. Allaway, G.P., K.L. Davis-Bruno, B.A. Beaudry, E.B. Garcia, E.L. Wong, A.M. Ryder, K.W. Hasel, M.C. Gauduin, R.A. Koup, J.S. McDougal and P.J. Maddon. 1995. Expression and characterization of CD4-IgG2, a novel heterotetramer that neutralizes primary HIV type 1 isolates. AIDS Res Hum Retroviruses 11: 533-539 (Exhibit 1).

2. Allaway, G.P., A.M. Ryder, G.A. Beaudry and P.J. Maddon. 1993. Synergistic inhibition of HIV-1 envelope-mediated cell fusion by CD4-based molecules in combination with antibodies to gp120 or gp41. AIDS Res Hum Retroviruses 9: 581-587 (Exhibit 2).

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Applicants: William C. Olson, et al.
Serial No.: 09/464,902
Filed: December 16, 1999
Page 2

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3. Amara, A., S.L. Gall, O. Schwartz, J. Salamero, M. Montes, P. Loetscher, M. Baggiolini, J.L. Virelizier and F. Arenzana-Seisdedos. 1997. HIV coreceptor downregulation as antiviral principle: SDF-1 α -dependent internalization of the chemokine receptor CXCR4 contributes to inhibition of HIV replication. *J. Exp. Med.* 186: 139-146 (Exhibit 3).
4. Berger, E.A. 1997. HIV entry and tropism: the chemokine receptor connection. *AIDS* 11 (suppl A): S3-S16 (Exhibit 4).
5. Bieniasz, P.D., R.A. Fridell, I. Aramori, S.S.G. Ferguson, M.C. Caron and B.R. Cullen. 1997. HIV-1-induced cell fusion is mediated by multiple regions within both the viral envelope and the CCR5 co-receptor. *EMBO* 16: 2599-2609 (Exhibit 5).
6. Brelo, A., N. Heveker, O. Pleskoff, N. Sol and M. Alizon. 1997. Role of the first and third extracellular domains of CXCR4 in human immunodeficiency virus coreceptor activity. *J. Virol.* 71: 4744-4751 (Exhibit 6).
7. Chan, D.C. and P.S. Kim. 1998. HIV entry and its inhibition. *Cell* 93: 681-684 (Exhibit 7).
8. Connor, R.I., K.E. Sheridan, D. Ceradini, S. Choe and N.R. Landau. 1997. Change in co-receptor use correlates with disease progression in HIV-1 infected individuals. *J. Exp. Med.* 185: 621-628 (Exhibit 8).
9. Crump, M.P., J.H. Gong, P. Loetscher, K. Rajarathnam, A. Amara, F. Arenzana-Seisdedos, J.L. Virelizier, M. Baggiolini, B.D. Sykes and I. Clark-Lewis. 1997. Solution structure and basis for functional activity of stromal-cell derived factor-

Applicants: William C. Olson, et al.
Serial No.: 09/464,902
Filed: December 16, 1999
Page 3

1; disassociation of CXCR4 activation from binding and inhibition of HIV-1. EMBO 16: 6996-7007 (Exhibit 9).

10. Dalgleish, A.G., P.C.L. Beverly, P.R. Clapham, D.H. Crawford, M.F. Greaves and R.A. Weiss. 1984. The CD4 (T4) antigen is an essential component of the receptor for the AIDS retrovirus. Nature 312: 763-766 (Exhibit 10).
11. Donzella, G.A., D. Schols, S.W. Lin, J.A. Este, K.A. Nagashima, P.J. Maddon, G.P. Allaway, T.P. Sakmar, G. Henson, E.D. Clercq and J.P. Moore. 1998. AMD3100, a small molecule inhibitor of HIV-1 entry via the CXCR4 co-receptor. Nat. Med. 4: 72-77 (Exhibit 11).
12. Doranz, B.J., K. Grovit-Ferbas, M.P. Sharron, S.H. Mao, M.B. Goetz, E.S. Daar, R.W. Doms and W.A. O'Brien. 1997. A small molecule inhibitor directed against the chemokine receptor CXCR4 prevents its use as an HIV-1 co-receptor. J. Ex. Med. 186: 1395-1400 (Exhibit 12).
13. Doranz, B.J., Z.-H. Lu, J. Rucker, T.-Y. Zhang, M. Sharron, Y.-H. Cen, Z.-X. Wang, H.-H. Guo, J.-G. Du, M.A. Accavitti, R.W. Doms and S.C. Peiper. 1997. Two distinct CCR5 domains can mediate co-receptor usage by human immunodeficiency virus type 1. J. Virol. 71: 6305-6314 (Exhibit 13).
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Applicants: William C. Olson, et al.
Serial No.: 09/464,902
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Page 4

JUN 26 2000

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16. Kwong, P.D., R. Wyatt, J. Robinson, R.W. Sweet, J. Sodroski and W.A. Hendrickson. 1998. Structure of an HIV gp120 envelope glycoprotein in complex with the CD4 receptor and a neutralizing human antibody. *Nature* 393: 648-659 (Exhibit 16).
17. Laal, S., S. Burda, M.K. Gorny, S. Karwowska, A. Buchbinder and S. Zolla-Pazner. 1994. Synergistic neutralization of human immunodeficiency virus type 1 by combinations of human monoclonal antibodies. *J. Virol.* 68: 4001-4008 (Exhibit 17).
18. Li, A., H. Katinger, M.R. Posner, L. Cavacini, S. Zolla-Pazner, M.K. Gorny, J. Sodroski, T.C. Chou, T.W. Baba and R.M. Ruprecht. 1998. Synergistic neutralization of simian-human immunodeficiency virus SHIV-vpu+ by triple and quadruple combinations of human monoclonal antibodies and high-titer antihuman immunodeficiency virus type 1 immunoglobulins. *J. Virol.* 72: 3235-3240 (Exhibit 18).
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Applicants: William C. Olson, et al.
Serial No.: 09/464,902
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20. McKnight, A., D. Wilkinson, G. Simmons, S. Talbot, L. Picard, M. Ahuja, M. Marsh, J.A. Hoxie and P.R. Clapham. 1997. Inhibition of human immunodeficiency virus fusion by a monoclonal antibody to a coreceptor (CXCR3) is both cell type and virus strain dependent. *J. Virol.* 71: 1692-1696 (Exhibit 20).
21. Strizki, J.M., J. Davis-Turner, R.G. Collman, J. Hoxie and F. Gonzalez-Scarano. 1997. A monoclonal antibody (12G5) directed against CXCR4 inhibits infection with the dual-tropic human immunodeficiency virus type 1 isolate HIV-1 89.6 but not the T-tropic isolate HIV-1 HxB. *J. Virol.* 71: 5678-5683 (Exhibit 21).
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23. Vijh-Warrier, S., A. Pinter, W.J. Honnen and S.A. Tilley. 1996. Synergistic neutralization of human immunodeficiency virus type 1 by a chimpanzee monoclonal antibody against the V2 domain of gp120 in combination with monoclonal antibodies against the V3 loop and the CD4-binding site. *J. Virol.* 70: 4466-4473 (Exhibit 23).
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Applicants: William C. Olson, et al.
Serial No.: 09/464,902
Filed: December 16, 1999
Page 6

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26. Tilley, S. A., W.J. Honnen, S. Warrier, M.E. Rach, T.C. Chou, M. Girard, E. Muchmore, M. Hilgartner, D.D. Ho, M.S.C. Fung, and A. Pinter. 1991. Potent Neutralization of HIV-1 by Human and Chimpanzee Monoclonal Antibodies Directed Against Three Distinct Epitope Clusters of gp120. Sixieme Colloque Des Cent Gardes. 211-216 (Exhibit 26)
27. Tilley, S.A., W.J. Honnen, M.E. Rach, T.C. Chou, and A. Pinter. 1992. Synergistic Neutralization of HIV-1 by Human Monoclonal Antibodies Against the V3 Loop and the CD4-Binding Site of gp120. AIDS Research and Human Retroviruses 80:4: 461-467 (Exhibit 27)
28. Choe, H., M. Farzan, Y. Sun, N. Sullivan, B. Rollins, P.D. Ponath, L. Wu, C.R. Mackay, G. LaRosa, W. Newman, N. Gerard, C. Gerard, and J. Sodroski. The Beta-Chemokine Receptors CCR3 and CCR5 Facilitate Infection by Primary HIV-1 Isolates. Cell 85: 1135-1148 (Exhibit 28)
29. Doranz, B.J., J. Rucker, Y. Yi, R. Smyth, M. Samson, S.C. Peiper, M. Parmentier, R.G. Collman, and R.W. Doms. A Dual-Tropic Primary HIV-1 Isolate That Uses Fusin and Beta-Chemokine Receptors CKR-5, CKR-3, and CKR-2b as Fusion Cofactors. Cell 85: 1149-1158 (Exhibit 29)

Applicants: William C. Olson, et al.
Serial No.: 09/464,902
Filed: December 16, 1999
Page 7

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31. Feng, Y., C.C. Broder, P.E. Kennedy, E.A. Berger. HIV-1 Entry Cofactor: Functional cDNA Cloning of a Seven-Transmembrane, G Protein-Coupled Receptor. *Science* 272: 872-877 (Exhibit 31)

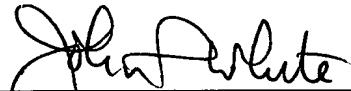
PCT International Application No. PCT/US99/30345, filed December 16, 1999, is a foreign counterpart application of the subject application. A search report was issued on June 7, 2000 in connection with PCT/US99/30345. A copy of the Search Report is attached hereto as **Exhibit B**. Above listed references 2, 14, and 26-31 were cited in the search report.

Applicants: William C. Olson, et al.
Serial No.: 09/464,902
Filed: December 16, 1999
Page 8

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invite the Examiner to telephone him at the number provided below.

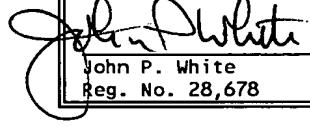
Pursuant to 37 C.F.R. §1.97(b)(3) no fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this paper is being deposited this date with the U.S. Postal Service as first class mail addressed to:
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